Clinical Rehabilitation 2006; **20:** 311–323

Nutritional supplementation and resistance training in nutritionally at risk older adults following lower limb fracture: a randomized controlled trial

Michelle D Miller, Maria Crotty and **Craig Whitehead** Flinders University Department of Rehabilitation and Aged Care and **Elaine Bannerman** and **Lynne A Daniels** Flinders University Department of Nutrition and Dietetics, South Australia

Received 28th July 2005; returned for revisions 16th September 2005; revised manuscript accepted 21st October 2005.

Objective: To describe the independent and combined effects of oral nutrition supplementation and resistance training on health outcomes in nutritionally at risk older adults following lower limb fracture.
Design: Randomized controlled trial with 12-week masked outcome assessment.
Setting: Teaching hospital.
Participants: One hundred nutritionally at risk older adults hospitalized following a fall-related lower limb fracture.
Intervention: Commenced seven days after injury. Consisted of daily multinutrient energy-dense oral supplement (6.3 kJ/mL) individually prescribed for six weeks ($n = 25$), tri-weekly resistance training for 12 weeks ($n = 25$), combined treatment ($n = 24$) or attention control plus usual care and general nutrition and exercise advice ($n = 26$).
Measurements: Weight change, quadriceps strength, gait speed, quality of life and health care utilization at completion of the 12-week intervention.
Results: At 12 weeks, all groups lost weight: nutrition −6.2% (−8.4, −4.0); resistance training −6.3% (−8.3, −4.3); nutrition and resistance training −4.7% (−7.4, −2.0); attention control −5.2% (−9.0, −1.5). Those receiving resistance training alone lost more weight than those receiving the combined treatment ($P = 0.029$). Significant weight loss was prevented if supplement was consumed for at least 35 days. Groups were no different at 12 weeks for any other outcome.
Conclusion: Frail, undernourished older adults with a fall-related lower limb fracture experience clinically significant weight loss that is unable to be reversed with oral nutritional supplements. Those receiving a programme of resistance training without concurrent nutrition support are at increased risk of weight loss compared with those who receive a combined nutrition and resistance training intervention. In this high-risk patient group it is possible to prevent further decline in nutritional status using oral nutritional supplements if strategies are implemented to ensure prescription is adequate to meet energy requirements and levels of adherence are high.

Address for correspondence: Maria Crotty, Flinders University Department of Rehabilitation and Aged Care, Repatriation General Hospital, Daws Road, Daw Park, South Australia.
e-mail: maria.crotty@flinders.edu.au

10.1191/0269215506cr942oa

Introduction

Fall-related osteoporotic fractures are a major cause of disability and loss of independence for older adults. Most of the burden is due to lower limb fractures and in particular hip fractures, which increase exponentially with age.[1] Hip fractures have serious medical and social consequences for older people, with recent United States research suggesting that hip fracture reduces life expectancy by 25%, 13% of patients move from the community to residential care and that estimated lifetime cost for the United States in 1997 probably exceeded $20 billion.[2]

Undernutrition is an important and amendable predictor of morbidity and mortality in older adults, as well as a risk factor for osteoporosis and fall-related fractures.[3] Between 39% and 65% of elderly patients admitted to hospital with a fractured hip show evidence of protein–energy undernutrition.[4,5] In hospital the situation is likely to deteriorate as the energy and protein intake of orthopaedic patients is often well below recommended requirements.[6] Undernutrition may impair recovery from lower limb fracture and has been associated with increased incidence of complications and infection, length of hospital stay and mortality.[7–12]

In the clinical setting, nutritional status in older patients at admission to hospital and beyond is largely ignored.[13] Oral nutritional supplements may be prescribed to maintain or improve nutritional status[14] but consumption is notoriously low when offered as an optional between-meal beverage as is common practice in many hospitals.[15] Many clinicians consider some form of nutritional supplements for hip fracture patients a matter of routine although a recent systematic review identifies the supporting evidence as weak.[16] Although some studies are positive others fail to show improvements in outcome. This discrepancy may be due to insufficient provision of energy and protein to preserve lean body mass and promote muscle strengthening. The physiological response to negative energy balance is use of protein stores (primarily skeletal muscle) for energy metabolism and hence the potential for improved muscle mass and strength becomes restricted.[17]

Decreased muscle mass and strength is associated with increased risk of falls and susceptibility to injury and lower limb fracture.[18–20] Randomized controlled trials examining strength and balance retraining exercise programmes have shown reductions in falls[21] and a small study of hip fracture patients has suggested that strengthening hip and knee muscles may improve mobility.[22]

Despite established associations and potential interactions between nutrition, mobility, strength and strength-related functional outcomes, there have been no randomized controlled trials amongst older adults that approximate usual clinical practice immediately following a lower limb fracture and where a combination of both nutrition and resistance training are provided.

Randomized controlled trials of oral nutrition supplementation following hip fracture incorporate a range of important outcomes, including achievement of rehabilitation goals,[23] indicators of muscle strength[24] and functional performance.[24–27] Randomized controlled trials of physical therapy following hip fracture[22,28–31] by contrast generally do not consider nutrition outcomes. Understanding changes to nutritional status is critical to understanding the effectiveness of these therapies.

The aim of this study was to determine the independent and combined effects of oral nutritional supplementation and resistance training on weight, quadriceps strength, gait speed, quality of life and health care utilization in a sample of nutritionally at risk older adults with a recent lower limb fracture.

Methods

Participants

All participants were recruited from the orthopaedic wards of the Flinders Medical Centre, Adelaide, South Australia. Patients aged ≥ 70 years consecutively admitted to Flinders Medical Centre with a fall-related lower limb fracture between September 2000 and October 2002 were screened for inclusion in the study. Patients were excluded who (1) did not reside within southern Adelaide, (2) were unable to comprehend instructions relating to positioning of the upper arm for eligibility assessment, (3) were unable to fully-weight bear on the side of the injury for more than

seven days post admission, (4) were not independently mobile prefracture, (5) were medically unstable > seven days post admission, (6) were suffering from cancer, chronic renal failure, unstable angina or unstable diabetes or (7) were not classified as malnourished, ($\geq$ 25th percentile for mid-arm circumference of a large representative sample of older Australians – 27.0 cm and 26.3 cm for males and females respectively).[32] Mid-arm circumference was used as a practical alternative to body mass index for eligibility screening due to the practical difficulties in obtaining accurate weight and particularly height without discomfort in older patients immediately following lower limb fracture and/or surgery. The World Health Organization recommends the use of mid-arm circumference for screening older adults for nutritional interventions.[33]

The study was approved by the Flinders Medical Centre Clinical Research and Ethics Committee and written informed consent was obtained from each participant or next of kin in the presence of cognitive impairment.

Randomization

Participants were randomized by using a stratified (admission accommodation: community or residential care), block randomization method (blocks of 12) following baseline assessment. The Pharmacy Department maintained a computer-generated allocation sequence in sealed opaque envelopes.

Trial interventions

Participants were randomized to receive usual clinical care (including general nutrition and exercise advice, usual dietetic and physiotherapy care, transfer to residential care, rehabilitation facility or directly home) in addition to treatment incorporating oral nutrition supplementation and/or resistance training. Interventions commenced seven days following fracture and were individually prescribed and supervised.

Nutrition supplementation

Fortisip (Nutricia Australia Pty Ltd), a complete oral nutritional supplement (6.3 kJ (1.5 kcal)/mL, 16% protein, 35% fat and 49% carbohydrate) was chosen as the oral nutritional supplement for the study. At the time the study was performed Fortisip was the only commercially manufactured, complete energy-dense supplement with a comprehensive range of flavours available in Australia. A single oral nutritional supplement was chosen for the study as there is evidence to suggest that using a variety of supplements from different manufacturers does not achieve high levels of adherence[34] and use of a single oral nutritional supplement is common practice in similar trials.[16] Fortisip was prescribed to cover the shortfall between individual estimated energy requirements and literature estimates of dietary intake in elderly hip fracture patients.[8,35] Individual theoretical energy requirements were based on the Schofield equation to estimate basal metabolic rate,[36] with adjustments for physical activity (1.2), trauma (1.35) and weight gain (0.25 kg/week).[37] The literature reports average daily energy intake as approximately 55–65% of these estimated requirements. Hence, supplement volumes were prescribed to meet 45% of individually estimated total energy requirements (i.e. shortfall between estimated energy requirements and literature estimates of energy intake) and ranged from 580 to 800 mL per day.

Four doses of equal volume of supplement were administered daily from the drug trolley on medication rounds by nursing staff. Volume prescribed and consumed was documented at each dose. On discharge from hospital, those admitted to residential care received the supplement as described for the hospital setting. For those discharged home scheduling (twice a day or more, daily volume constant) was negotiated with the participant and/or next of kin or carer. Volume of supplement consumed was recorded at each dose using a standardized format in a trial diary. Research staff checked the intake record and made a count of supplement packages at tri-weekly visits for the six-week intervention to confirm adherence. Adherence is reported as the median daily supplement consumption calculated over the 42 days of the intervention and expressed as a percent of daily volume prescribed. The duration of the nutrition supplementation was determined following a review of the literature which suggested that the most common duration (10–38 days) was not sufficient to achieve positive outcomes.[8,9,23,38] Weekly visits from weeks 7 to 12 were provided to match the participant contact in the resistance training intervention.

Resistance training

The training was supervised by a physiotherapist three times per week, 20–30 min per session, for 12 weeks. To ensure the resistance training intervention was standardized, the trial physiotherapists were instructed to deliver only the structured programme of therapy to participants. The programme incorporated progressive resistance training (using latex-free resistive elastic bands: REP Band, Magister Corporation, Chattanooga, TN, USA) of the hip extensors and abductors (supine), knee extensors (supine or sitting) and ankle dorsi- and plantar-flexors (supine or sitting). The frequency and duration of the resistance training programme was determined following a review of literature which suggested that positive outcomes could be achieved with tri-weekly training for between eight and 15 weeks.[39–43]

Commencing resistance was appropriate to baseline strength, pain level and range of movement of both the injured and non-injured limb. It was increased as soon as two sets of eight repetitions of the exercise could be completed in good form, determined on an individual basis at the discretion of the physiotherapist. Adherence and progression were documented by the physiotherapist, the participants and/or carer/next of kin using a standardized format in a trial diary. Adherence is reported as the number of sessions completed of those prescribed (total sessions = 36) multiplied by 100.

Attention control

To account for the possibility of an attention effect[44] this group received tri-weekly visits (of equivalent duration) weeks 1–6 and then weekly visits weeks 7–12, to match the home visits of the active intervention groups. Discussions during these visits were limited to general information (e.g. benefits of regular exercise and nutrient-dense meals). All participants were encouraged to continue treatments as prescribed during the hospital admission or by their treating health professionals.

Measurements and procedures

Medical records provided baseline demographic and clinical data prior to randomization including age, gender, prefracture living accommodation and type of fracture. Baseline cognition was determined using the Short Portable Mental Status Questionnaire (SPMSQ),[45] quality of life using the Short Form 12[46] and premorbid functional ability using the Modified Barthel Index.[47] At discharge from hospital, medical records were used to determine discharge destination and hospital length of stay.

Mid-arm circumference ($\pm$0.1 cm), weight ($\pm$0.1 kg) and knee height ($\pm$0.1 cm) were measured using standard equipment and procedures.[33] Stature, estimated from knee height,[48] was used to calculate the estimated body mass index (eBMI: kg/m^2).[49] Quadriceps strength ($\pm$0.1 kg) was measured using a hand-held Nicholas Manual Muscle Tester (Lafayette Instrument, Lafayette, IN, USA). Assessment of quadriceps strength was performed with the leg flexed at the hip and knee to 90° and the manual muscle tester placed on the distal tibia immediately proximal to the ankle joint along the line of the tibia. The participant was instructed to attempt to extend their knee by pushing their ankle outwards through the manual muscle tester whilst the assessor applied sufficient force to prevent movement. The test procedure was repeated three times (15 s intervals) on each leg.

Venous blood was analysed for 25-hydroxycholecalciferol (vitamin D) by immunoassay (Immuno Diagnostic Systems Ltd, Boldon, UK). Dietary intake was assessed using a plate waste method for up to five consecutive days following consent (days 6–11) and energy intake calculated using a dietary analysis program (SERVE Nutrition Management Systems for Microsoft Windows Version 3.0, 2000; SERVE Nutrition Management Systems, Sydney, Australia).

Research staff blinded to treatment allocation performed outcome assessments (weight, quadriceps strength, gait speed, quality of life) 12 weeks after commencement of trial interventions. Gait speed (not measured at baseline due to inability of patients to mobilize comfortably) was measured as the time (seconds) taken to walk the middle 10 m of a 15-m walk using a Sportline 240 Econosport Stopwatch (Sportline, USA). Participants were instructed to walk using their usual aids and at their normal walking pace and were provided with several metres to accelerate and decelerate before and after the test distance. Weight was also collected at the weekly visits by the visiting therapist.

Statistical analysis

All data were analysed using the SPSS statistical package (SPSS for Windows, Advanced Statistics, version 11.5.0 2002; SPSS Inc, Chicago, USA). Descriptive statistics were calculated according to treatment group (baseline and 12 weeks), values are reported as median or mean (95% confidence interval). Analyses were performed using an intention to treat approach.

A total sample size of 100 patients (25 per group) was projected to provide power of 80% with alpha = 0.05 to detect a clinically meaningful 5% difference in weight change[23,50] between at least one pair of the four groups. The trial was not powered to detect an interactive effect between the nutrition and resistance training intervention.

Differences across treatment groups were analysed using analysis of variance (ANOVA) for normally distributed data, Kruskal–Wallis for non-parametric continuous data and chi-square tests of association for categorical data. Data were conditionally missing at random and therefore imputation was performed using expectation–maximization (EM) algorithm.

Percentage weight change from baseline (day 7 post injury) was calculated. Negative values represent weight loss, positive values represent weight gain. Missing values were not imputed as no other variables were measured on a weekly basis. A linear mixed modelling procedure[51] was fitted to prevent cases with missing data being deleted and to look at differences across treatment groups: week 1–week 6, week 7–week 12 and week 1–week 12. Where a group effect was significant Bonferroni post-hoc tests were performed. To determine whether percentage weight change in the first six weeks was similar to the change observed in the second six weeks according to treatment group, repeated measures ANOVA (Bonferroni post-hoc tests) was performed.

Results

Recruitment and retention of participants

Recruitment, randomization and retention of participants are described in Figure 1. One hundred patients provided consent (67% of total eligible). Reasons for not consenting included too many visits ($n = 14$), too unwell ($n = 7$), family concern for demands on patient ($n = 5$) and inability to contact next of kin within seven days ($n = 5$). There were no significant differences between those identified as eligible who agreed or refused to consent. Ninety-three per cent completed the study to 12 weeks and there was no difference in the level of retention between treatment groups, $P = 0.872$.

Baseline characteristics, nutrient intake and discharge destination

Table 1 presents baseline characteristics of participants according to treatment group. Statistical comparisons indicated the groups were well matched. Mean (95% confidence interval (CI)) age of participants was 83.5 (82.3, 84.7) years, 79% were female, 76% were admitted to hospital from the community and 86% had suffered a fall-related fractured neck of femur. According to the SPMSQ, 48% of participants had cognitive impairment. Participants reported a high level of independence in ADL prior to fracture (Modified Barthel Index 100, 95% CI 98, 100). Mean (95% CI) estimated body mass index, mid-arm circumference and vitamin D status were 22.1 kg/m^2 (21.6, 22.7), 22.6 cm (22.1, 23.0) and 36 nmol/L (32, 43) respectively. During admission to the acute care setting, 28 participants were referred for dietetic intervention as part of usual care (nutrition $n = 6$, exercise $n = 6$, nutrition and exercise $n = 5$, attention control $n = 11$, $P = 0.302$).

Excluding supplements, participants consumed $68 \pm 20\%$ estimated energy requirements adjusted for activity level and this reduced to only $44 \pm 13\%$ when requirements were adjusted for activity level, skeletal trauma and weight gain. There was no significant change in the level of energy intake across the five days of data collection, $P = 0.790$.

On discharge from acute care 52 participants were discharged to a rehabilitation programme, 12 were transferred to a community hospital, 16 were discharged to higher level care and 20 returned directly to their pre-injury admission accommodation.

Treatment effects

Cumulative percentage weight change during weeks 1–6, 7–12 and over the whole intervention

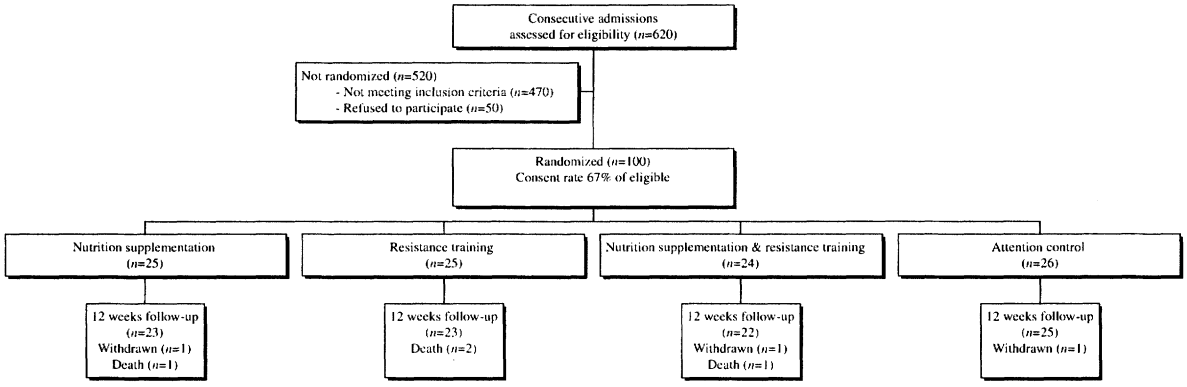

Figure 1 Recruitment, randomization and progression of nutritionally at risk patients aged ≥ 70 years who participated in a randomized controlled trial of oral nutritional supplements and progressive resistance training following a fall-related lower limb fracture.

period are shown in Table 2. For weeks 1–6 and weeks 7–12 there was a significant time effect ($F_{(5,301.9)} = 3.822$, $P = 0.002$; $F_{(5,196.6)} = 3.512$, $P = 0.005$ respectively) but only a significant group effect for weeks 1–6 ($F_{(3,96.0)} = 3.320$, $P = 0.023$), with Bonferroni post-hoc testing confirming participants allocated to resistance training lost more weight than those allocated to the combination of nutrition and resistance training, $P = 0.014$. The time and group effects were maintained over weeks 1–12 (time $F_{(11,440.3)} = 4.1$, $P < 0.001$; group $F_{(3,120.6)} = 2.9$, $P = 0.038$) and similarly Bonferroni post-hoc analysis confirmed greater weight loss in those allocated to resistance training compared to combined nutrition and resistance training, $P = 0.029$. According to repeated measures ANOVA, there was a significant time by group interaction ($P = 0.019$). Bonferroni post-hoc tests confirmed that those allocated to resistance training lost more weight in the first six weeks compared with the second six weeks (-5.2% versus -0.1%, $P = 0.003$).

Table 3 presents quadriceps strength, gait speed, quality of life and health care utilization outcomes across treatment group at 12 weeks. At 12 weeks all four treatment groups performed similarly for gait speed ($P = 0.933$), and quadriceps strength for both the injured and non-injured limb ($P = 0.493$ and $P = 0.894$ respectively). There were no significant differences in quality of life, readmission to hospital or admission to higher level care across treatment groups.

Adherence to the interventions

The median (95% CI) percentage of prescribed volume of nutritional supplement consumed daily calculated over the 42 days was 67% (46, 82) for the 49 participants who received supplement. There was no difference ($P = 0.496$) between the nutrition group ($n = 25$; 76% (44, 89)) and the nutrition and resistance training group ($n = 24$; 66% (38, 82)). Thirty-five of 49 participants consumed at least some supplement on 35 days or more and lost less weight than those who did not adhere (-0.7% versus -5.5%, $P = 0.003$). Adherence was correlated with percentage weight change ($r = 0.374$, $P = 0.011$). A detailed report of adherence to the oral nutritional supplement intervention has been described elsewhere.[52] Adherence to the 12 weeks resistance training intervention reached > 86% for all exercises performed.

Discussion

The results of the present study suggest that resistance training in undernourished older adults without concurrent nutrition support amplifies nutritional risk, potentially limiting the effectiveness of rehabilitation and synergistically compromising clinical outcomes. Cumulative weight loss for the combined nutrition and resistance training intervention was 4.7% compared with 6.3% in those receiving resistance training alone. Despite clinically significant weight loss across all treat-

Table 1 Baseline (prior to randomization) demographics, physical performance and self-report measures for 100 nutritionally at risk patients aged ≥ 70 years who participated in a randomized controlled trial of oral nutritional supplements and progressive resistance training following a fall-related lower limb fracture. All values are median (95% CI) unless otherwise stated

Characteristic	Treatment group[a]			
	Nutrition ($n = 25$)	Exercise ($n = 25$)	Nutrition and exercise ($n = 24$)	Attention control ($n = 26$)
Age (years), mean (95% CI)	83.5 (81.0, 86.0)	84.8 (82.3, 87.4)	82.7 (80.3, 85.0)	83.1 (80.5, 85.7)
Female, *n* (%)	21 (84%)	20 (80%)	17 (71%)	21 (81%)
Living at home, *n* (%)	19 (76%)	19 (76%)	19 (79%)	19 (73%)
Fractured neck of femur[b], *n* (%)	23 (92%)	21 (84%)	22 (92%)	20 (77%)
Impaired cognition[c], *n* (%)	11 (44%)	12 (48%)	8 (33%)	17 (65%)
Length of hospital stay (days)				
Acute	10.0 (6.0, 17.0)	11.0 (8.0, 17.0)	10.0 (7.0, 12.0)	12.0 (6.0, 22.0)
Rehabilitation[d]	18.0 (13.0, 23.0)	21.5 (10.0, 62.0)	22.0 (16.0, 34.0)	17.0 (14.0, 39.0)
Total	24.0 (18.0, 29.0)	23.0 (16.0, 32.0)	27.5 (13.0, 31.0)	24.0 (17.0, 30.0)
Nutritional health				
Weight (kg), mean (95% CI)	53.0 (49.5, 56.6)	52.3 (48.2, 56.4)	57.5 (54.4, 60.6)	54.7 (50.3, 59.0)
Estimated body mass index (kg/m^2)[e]				
Mean (95% CI)	21.9 (20.8, 23.0)	21.4 (20.4, 22.4)	23.2 (22.2, 24.2)	22.1 (20.6, 23.6)
n (%) < desirable[f]	14 (56%)	13 (52%)	7 (29%)	13 (50%)
Vitamin D (nmol/L)	41 (33, 52)	32 (29, 47)	41 (28, 55)	32 (30, 45)
n (%) < desirable[g]	12 (48%)	15 (60%)	11 (46%)	17 (65%)
Physical performance				
Quadriceps strength, kg (injured)	2.7 (1.6, 3.9)	1.6 (0.8, 3.0)	3.0 (1.4, 3.6)	1.8 (1.0, 3.8)
Quadriceps strength, kg (non-injured)	4.9 (3.5, 6.5)	4.3 (2.2, 5.8)	4.9 (3.5, 6.7)	5.2 (1.9, 6.5)
Modified Barthel Index[h], (range 0–100)	100 (96, 100)	100 (95, 100)	100 (98, 100)	100 (90, 100)
Quality of life[i]				
SF-12 – physical (range 24–56)	35.8 (26.8, 44.7)	38.9 (35.0, 47.8)	33.9 (28.9, 53.2)	38.0 (29.9, 46.0)
SF-12 – mental (range 19–60)	54.0 (43.3, 57.2)	53.4 (49.1, 57.2)	45.9 (41.0, 57.3)	46.1 (39.3, 53.3)

95% CI, 95% confidence interval.

[a] Treatment groups consisted of either six weeks of an individually prescribed volume of a 6.3 kJ/mL oral nutritional supplement (nutrition), a 12 weeks resistance training programme (exercise), a combination (nutrition and exercise) or attention control. Comparison across treatment groups were calculated using one-way ANOVA for normally distributed continuous data, Kruskal–Wallis test for non-parametric continuous data and chi-square test of association for categorical variables. No significant differences were identified across the four treatment groups.

[b] Other fracture types included femur, tibia, fibula ($n = 8$) or pelvic ($n = 6$).

[c] Cognition assessed using the Short Portable Mental Status Questionnaire.[45]

[d] Only calculated for subjects admitted to a rehabilitation facility or rehabilitation in the home, $n = 52$ (nutrition = 16; exercise = 10; nutrition and exercise = 14; attention control = 12).

[e] Stature estimated from measurement of knee height.[48]

[f] Estimated body mass index ≥ 22 kg/m^2 = desirable.[61]

[g] Vitamin D 40–160 nmol/L = desirable.

[h] Modified Barthel Index.[47]

[i] Quality of life assessed using the Short Form 12 (SF-12).[46]

ment groups, the present study shows that it is possible to achieve weight maintenance in this frail patient group if strategies are implemented to ensure the nutrition supplement prescription is adequate to achieve energy balance and levels of adherence are high.

Of nine published oral nutritional support trials in hip fracture patients,[8,9,23–27,38,53] a variety of positive outcomes are reported, including reduced length of stay, reduced complications and improved fatigue. However, these studies as a whole present conflicting and inconsistent results. This variability may be due to these studies failing to account for the imbalance between metabolic requirements and supplement prescribed. Only two of these studies have reported weight change

Table 2 Mean (95% CI) percentage weight change for 100 nutritionally at risk patients aged ≥ 70 years who participated in a randomized controlled trial of oral nutritional supplements and progressive resistance training following a fall-related lower limb fracture

Percentage weight change[b]	Treatment group[a]				*P*-value
	Nutrition	Exercise	Nutrition and exercise	Attention control	
Week 1–week 6	−2.6 (−4.7, −0.5)	−5.2 (−7.6, −2.8)	−0.9 (−2.8, 1.0)	−1.8 (−4.0, 0.3)	0.023[d]
n (%) ≥ 5%[c]	7 (28)	11 (44)	4 (17)	7 (27)	
Week 7–week 12	−3.2 (−5.4, −1.0)	−0.1 (−2.3, 2.1)	−2.9 (−5.0, −0.9)	−3.4 (−7.0, 0.3)	0.163
n (%) ≥ 5%[c]	5 (20)	4 (16)	7 (30)	6 (23)	
Week 1–week 12	−6.2 (−8.4, −4.0)	−6.3 (−8.3, −4.3)	−4.7 (−7.4, −2.0)	−5.2 (−9.0, −1.5)	0.038[e]
n (%) ≥ 5%[d]	13 (52)	14 (56)	12 (50)	12 (46)	

95% CI, 95% confidence interval.
[a] Treatment groups consisted of either six weeks of an individually prescribed volume of a 6.3 kJ/mL oral nutritional supplement (nutrition), a 12 weeks resistance training programme (exercise), a combination (nutrition and exercise) or attention control. Comparison across treatment groups calculated using a linear mixed modelling procedure.[51]
[b] Denominator altered as missing data were not imputed: baseline ($n = 100$), end of week 1 ($n = 99$), week 2 ($n = 98$), weeks 3, 4, 5, 6 ($n = 96$), week 7 ($n = 93$), weeks 9 and 12 ($n = 93$), week 11 ($n = 91$), week 10 ($n = 90$).
[c] *N* (%) ≥ 5% refers to the number and percentage of participants that lost ≥ 5% body weight for a given time period.
[d] Post-hoc Bonferroni test, nutrition and exercise significantly different to exercise, $P = 0.014$.
[e] Post-hoc Bonferroni test, nutrition and exercise significantly different to exercise, $P = 0.029$.

during the period of intervention.[23,26] The largest and most recent of these[26] reports clinically significant weight loss similar to the present study. In this quasi-randomized controlled trial, Bruce *et al.*[26] found that 28 days of an oral nutritional supplement (235 mL) was insufficient to prevent weight loss in 50 older women with a mean baseline BMI 23 kg/m^2 (day 2–3 post operatively). At the completion of the nutrition intervention, 32% of the total sample ($n = 109$) had lost more than 5% of their baseline body weight. This compares with 29% of the overall sample from the present study losing more than 5% of baseline weight (day 7 post injury) over the first six weeks of intervention, highlighting that clinically significant weight loss occurs even with individually prescribed oral nutrition supplementation.

Similar to the findings of Bruce *et al.*[26] the present study found more weight loss during the treatment period compared with the period immediately following, possibly suggesting a difference in energy expenditure over the two periods of time. This, however, is not consistent with the literature that suggests a hypermetabolic state can persist for three months after surgery.[54] Another plausible explanation might be that volitional dietary intake improves over time; however, factors influencing appetite of this patient group are poorly understood. Studies of food intake following hip fracture are mostly limited to the period immediately post operative[6,35] and due to issues of burden and validity of dietary intake assessment the present study did not measure intake at follow-up and therefore is unable to explore this possibility further. There is also the possibility that the nutritional supplements displaced volitional intake and when the supplementation ceased participants did not respond with an increase in energy and protein intake from meals. However, the limited available evidence suggests that oral supplements in hip fracture patients do not significantly reduce volitional dietary intake.[8]

Strength, quality of life and health care utilization outcomes assessed in the present study were not altered significantly by the intervention. This is not surprising since the results of the present study suggested that participants remained in negative energy balance until at least 12 weeks post injury. The prescription of nutritional supplements in the present study was based on energy requirements estimated using standard predictive equations established on very small numbers of older adults.[36] The actual dose required to achieve positive energy balance remains unclear. However,

Table 3 Comparison of outcomes at 12 weeks follow-up for 100 nutritionally at risk patients aged ≥70 years who participated in a randomized controlled trial of oral nutritional supplements and progressive resistance training following a fall-related lower limb fracture. Values represent median (95% CI) unless otherwise stated

Outcome	Treatment group[a]			
	Nutrition ($n=25$)	Exercise ($n=25$)	Nutrition and exercise ($n=24$)	Attention control ($n=26$)
Physical performance				
Gait speed, m/s	0.5 (0.2, 0.6)	0.4 (0.3, 0.6)	0.3 (0.2, 0.7)	0.5 (0.3, 0.6)
Quadriceps strength, kg (injured limb)	4.5 (3.3, 5.9)	5.2 (3.8, 6.2)	5.7 (4.6, 7.6)	5.1 (3.4, 7.6)
Mean (95% CI) Δ from baseline	2.3 (1.0, 3.7)	3.6 (2.2, 5.0)	3.3 (2.1, 4.5)	2.7 (1.3, 4.0)
Quadriceps strength, kg (non-injured limb)	6.5 (3.6, 8.8)	5.2 (3.7, 7.0)	6.8 (5.8, 8.8)	4.8 (4.3, 7.2)
Mean (95% CI) Δ from baseline	1.1 (−0.2, 2.5)	1.7 (−0.0, 3.4)	1.5 (0.0, 3.1)	1.0 (−0.3, 2.4)
Quality of life[b]				
SF-12 physical component score, (range 24–56)	31.6 (29.5, 37.3)	31.5 (28.2, 41.9)	26.9 (22.6, 38.5)	30.1 (26.3, 36.3)
Mean (95% CI) Δ from baseline	−4.3 (−9.1, 0.5)	−5.5 (−9.3, −1.7)	−7.8 (−12.9, −2.7)	−6.0 (−10.5, −1.5)
SF-12 mental component score, (range 19–60)	51.4 (43.8, 60.1)	51.3 (46.5, 57.8)	49.8 (46.8, 58.3)	49.5 (41.1, 58.8)
Mean (95% CI) Δ from baseline	1.0 (−2.8, 4.7)	−1.2 (−5.0, 2.7)	3.1 (−2.7, 9.0)	4.5 (0.2, 8.8)
n (%) Readmitted to hospital[c]	2 (9%)	3 (13%)	2 (9%)	4 (16%)
n (%) Admitted to higher level care[c]	4 (17%)	5 (22%)	6 (27%)	6 (24%)

95% CI, 95% confidence interval.

[a] Treatment groups consisted of either six weeks of an individually prescribed volume of a 6.3 kJ/mL oral nutritional supplement (nutrition), a 12 weeks resistance training programme (exercise), a combination (nutrition and exercise) or attention control. Comparison across treatment groups calculated using one-way ANOVA for normally distributed continuous data and Kruskal–Wallis test for non-parametric continuous data and chi-square test of association for categorical variables. No significant differences were identified across the four treatment groups.

[b] Quality of life assessed using the Short Form 12 (SF-12).[46]

[c] Only assessed for subjects available for follow-up at 12 weeks, $n=93$ (nutrition = 23; exercise = 23; nutrition and exercise = 22; attention control = 25).

in the present study participants were able to achieve greater volumes and therefore greater energy intake from the nutritional supplement than any previous studies in this patient group and in those that adhered, significant weight loss was prevented.

The adherence data from the present study show that weight remains relatively constant over 42 days for those that consumed supplement for ≥35 days, whilst those who consumed supplement for <35 days lost 5.5% of their baseline body weight. There was also a significant although moderate correlation between adherence and percentage weight change which suggested that as adherence to the nutritional supplement improved, the amount of weight change improved (less weight was lost). It is important to interpret the findings of this secondary analysis with caution as there may have been additional factors that influenced these results and a separate controlled trial would need to be conducted to determine a true causal relationship.

Older adults following hip fracture are a heterogeneous population but clinical interventions such as nutrition support tend to be protocol driven rather than individually tailored. The data of the present study suggest that this frail group need a more aggressive intervention to achieve improved outcomes. The sample of the present study was recruited sequentially, and included possibly the most frail of all those presenting to the orthopaedic ward as they were selected to be undernourished and there was no exclusion of patients presenting with cognitive impairment. It was hypothesized that these patients would have the most to gain from the study intervention.

The present study was powered to detect a difference in percentage weight change between the groups and one limitation in this trial is the relatively small sample size. This meant that the power to detect differences for other outcomes (e.g. functional) may have been reduced. Only two studies of oral nutritional supplementation have reported power calculations and the sample size of the present study was similar[53] or larger.[27] The study interventions were not implemented until day 7 post injury and there may have been significant declines or complications prior to commencing the interventions that impacted on the effectiveness of treatment. Timing of interventions following hip fracture is inconsistent with oral nutrition supplementation trials commencing anywhere between day 1 of admission to acute care[8] to day 1 of admission to rehabilitation (within three weeks)[27] and the earliest of the exercise interventions commencing at discharge from rehabilitation.[30] There are possibly other unknown non-medical variables that may have impacted on outcomes of all participants. Participation in research trials has been shown to impact positively on outcomes.[55] For ethical reasons the present study could not withdraw usual care from any participants referred for dietetic interventions. Although not statistically significant there were a larger number of participants in the attention control group that were referred for dietetic intervention. If these participants adhered to the interventions recommended and remained in hospital for a sufficient duration it is possible that this may have diluted any treatment effect of the interventions being evaluated. Collection of adherence to usual dietetic interventions was beyond the scope of this study, however evidence suggests that adherence to oral nutritional supplements is notoriously poor and the average acute length of stay for participants in the attention control group was only 12 days. Hence it is unlikely that allowing usual care to continue in the attention control group had any significant impact on the findings of the present study.

A limitation of the data presented here is the use of weight change as a main outcome as it may be confounded by postoperative and inflammatory response driven fluid balance changes. However, randomization should limit this confounding across the groups. Weight change has been identified as a nutritional outcome in several recent systematic reviews of nutrition support interventions[56–58] and significant weight loss is widely used as an indicator of nutritional screening and assessment.[59] In addition, weight change provides an indication of whether the intervention provides sufficient energy to meet requirements and achieve positive outcomes. Albumin has been used as the nutritional indicator in the majority of oral supplementation trials in hip fracture patients[16] but is also subject to confounding related to injury and surgery.[60]

Strengths of the study presented here are numerous. To our knowledge it is the first trial in this patient group to evaluate the effects of a combined nutrition and resistance training programme, similar to protocols used in many clinical settings. The interventions were individually prescribed and administered according to baseline nutritional status and strength, also approximating clinical practice. Patients were not discriminated against according to cognitive status and only those screened as nutritionally at risk were approached to participate, a protocol used to ensure that patients with the most to gain were not excluded. As previously noted, no studies have commenced an exercise programme in this patient group so soon after injury and adherence to the nutrition intervention achieved an intake higher in volume and nutrient density than any similar trials. It is also worth noting that the data presented was analysed using the principle of intention to treat, whilst all but two similar trials of oral nutritional

Clinical messages

- Undernourished older adults experience significant weight loss following lower limb fracture.
- Decline in nutritional status using oral supplements may be possible even if the prescription meets requirements and adherence is high.
- Alternative methods of feeding should be considered in those patients that do not adhere to oral supplements.

supplementation[23,53] have excluded cases with incomplete data.

In summary, the clinically significant weight loss observed across all treatment groups is concerning amongst this already nutritionally at risk clinical group and further research is needed to determine (a) the change in energy and nutrient requirements of this group during both acute and rehabilitation phases, (b) alternative strategies for delivery of sufficient energy and (c) the dosage of resistance training sufficient to improve muscle strength. Until positive energy balance and adequate nutritional status is achieved it is likely that studies will continue to observe a lack of clinical benefit from nutritional supplementation. The data presented here suggest that resistance training in nutritionally at risk patients without concurrent nutritional support may further compromise nutritional status. Given the potential for undernutrition to result in muscle wasting, reduced muscle power and work capacity and mental apathy,[14,16] we speculate that failure to ensure adequate protein and energy intake to correct existing undernutrition may limit the effectiveness of physical therapy (which further increases requirements) and synergistically impact negatively on overall clinical outcomes. Early and aggressive alternative methods such as tube feeding should be considered in hip fracture patients at nutritional risk to prevent further deterioration in nutritional status and the associated implications for those unable to achieve adequate energy intake through diet and oral nutritional supplements.

Acknowledgements

We are grateful for the assistance of all staff involved in recruitment, implementation of the interventions and outcome data collection. We also thank the Flinders University Statistician Kylie Lange for her statistical advice and the research subjects who volunteered to participate in this study.

This research was conducted with support from the following sources: NHMRC Public Health Postgraduate Research Scholarship, Flinders University-Industry Collaborative Research Grant and Nutricia Australia Pty Ltd.

References

1 Melton L. Epidemiology of hip fractures: implications of the exponential increase with age. *Bone* 1996; **18**(suppl): 121S–5S.
2 Braithwaite R, Col N, Wong J. Estimating hip fracture morbidity, mortality and costs. *J Am Geriatr Soc* 2003; **51**: 364-70.
3 Department of Health. *Report on health and social subjects 43: the nutrition of elderly people*. London: Her Majesty's Stationery Office, 1992.
4 Hanger HC, Smart EJ, Merrilees MJ *et al.* The prevalence of malnutrition in elderly hip fracture patients. *NZ Med J* 1999; **112**: 88–90.
5 Koval KJ, Maurer SG, Su ET *et al.* The effects of nutritional status on outcome after hip fracture. *J Orthop Trauma* 1999; **13**: 164–69.
6 Older M, Edwards D, Dickerson J. A nutrient survey in elderly women with femoral neck fractures. *Br J Surg* 1980; **67**: 884–86.
7 Patterson B, Cornell CN, Carbone B. Protein depletion and metabolic stress in elderly patients who have a fracture of the hip. *J Bone Joint Surg* 1992; **2**: 251–60.
8 Delmi M, Rapin CH, Bengoa JM *et al.* Dietary supplementation in elderly patients with fractured neck of the femur. *Lancet* 1990; **335**: 1013–16.
9 Tkatch L, Rapin CH, Rizzoli R *et al.* Benefits of oral protein supplementation in elderly patients with fracture of the proximal femur. *J Am Coll Nutr* 1992; **11**: 519–25.
10 Bastow MD, Rawlings J, Allison S. Benefits of supplementary tube feeding after fractured neck of femur: a randomised controlled trial. *BMJ* 1983; **287**: 1589–92.
11 Muhlethaler R, Stuck AE, Minder CE *et al.* The prognostic significance of protein and energy malnutrition in geriatric patients. *Age Ageing* 1995; **24**: 193–97.
12 Campbell A, Spears GFS, Brown JS *et al.* Anthropometric measurements as predictors of mortality in a community population aged 70 years and over. *Age Ageing* 1990; **19**: 131–35.
13 McWhirter J, Pennington C. Incidence and recognition of malnutrition in hospital. *BMJ* 1994; **308**: 5–8.
14 Green C. Existence, causes and consequences of diet-related malnutrition in the hospital and the community, and clinical and financial benefits of nutritional intervention. *Clin Nutr* 1999; **18**: 3–28.
15 Keele AM, Bray MJ, Emery PW *et al.* Two phase randomised controlled clinical trial of postoperative oral dietary supplements in surgical patients. *Gut* 1997; **40**: 393–99.

16 Avenell A, Handoll HHG. Nutritional supplementation for hip fracture aftercare in the elderly. *Cochrane Database Syst Rev* 2005; 2.
17 Tipton KD, Wolfe RR. Exercise, protein metabolism, and muscle growth. *Int J Sport Nutr Exerc Metab* 2001; **11**: 109–32.
18 Wolfson L, Judge J, Whipple R *et al.* Strength is a major factor in balance, gait, and the occurrence of falls. *J Gerontol A Biol Sci Med Sci* 1995; **50A**: 64–67.
19 Wickham C, Cooper C, Margetts B *et al.* Muscle strength, activity, housing and the risk of falls in elderly people. *Age Ageing* 1989; **18**: 47–51.
20 Nguyen T, Sambrook P, Kelly P *et al.* Prediction of osteoporotic fractures by postural instability and bone density. *BMJ* 1993; **307**: 1111–15.
21 Campbell A, Robertson MC, Gardner MM *et al.* Randomised controlled trial of a general practice program of home based exercise to prevent falls in elderly women. *BMJ* 1997; **315**: 1065–69.
22 Baker P, Evans O, Lee C. Treadmill gait retraining following fractured neck of femur. *Arch Phys Med Rehabil* 1991; **72**: 649–52.
23 Brown K, Seabrook N. Effect of nutrition on recovery after fractured femur. *Med Audit News* 1992; **2**: 10–12.
24 Schurch MA, Rizzoli R, Slosman D *et al.* Protein supplements increase serum insulin-like growth factor-1 levels and attenuate proximal femur bone loss in patients with recent hip fracture. *Ann Intern Med* 1998; **128**: 801–809.
25 Espaulella J, Guyer H, Diaz-Escriu F *et al.* Nutritional supplementation of elderly hip fracture patients. A randomized, double-blind, placebo-controlled trial. *Age Ageing* 2000; **29**: 425–31.
26 Bruce D, Laurance I, McGuiness M *et al.* Nutritional supplements after hip fracture: poor compliance limits effectiveness. *Clin Nutr* 2003; **22**: 497–500.
27 Neumann M, Friedmann J, Roy MA *et al.* Provision of high-protein supplement for patients recovering from hip fracture. *Nutrition* 2004; **20**: 415–19.
28 Sherrington C, Lord S. Home exercise to improve strength and walking velocity after hip fracture. *Arch Phys Med Rehabil* 1997; **78**: 208–12.
29 Tinetti ME, Baker DI, Gottschalk M *et al.* Home-based multicomponent rehabilitation program for older persons after hip fracture: a randomized trial. *Arch Phys Med Rehabil* 1999; **80**: 916–22.
30 Hauer K, Specht N, Schuler M *et al.* Intensive physical training in geriatric patients after severe falls and hip surgery. *Age Ageing* 2002; **31**: 49–57.
31 Binder E, Brown M, Sinacore D *et al.* Effects of extended outpatient rehabilitation after hip fracture. *JAMA* 2004; **292**: 837–46.
32 Andrews G. *The Australian Longitudinal Study of Ageing and a collaborative study of ageing in the US and Australia*. Adelaide: Flinders University of South Australia, 1992.
33 World Health Organization (WHO). *Physical status: the use and interpretation of anthropometry*. Report of a WHO Expert Committee, No. 854. Geneva: WHO, 1995.
34 Williams CM, Driver LT, Older J *et al.* A controlled trial of sip feed supplements in elderly orthopaedic patients. *Eur J Clin Nutr* 1989; **43**: 267–74.
35 Dickerson J, Fekkes J, Goodinson SM *et al.* Postoperative food intake of elderly fracture patients. In: Chandra RK, ed. *Nutrition, immunity and illness in the elderly*. Pergamon Press 1984; 247–452.
36 Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 1985; **39**(suppl 1): 5–41.
37 Long C, Schaffel N, Geiger JW *et al.* Metabolic response to injury and illness: estimation of energy and protein needs from indirect calorimetry and nitrogen balance. *J Parenter Enteral Nutr* 1979; **3**: 452–56.
38 Stableforth PG. Supplement feeds and nitrogen and calorie balance following femoral neck fracture. *Br J Surg* 1986; **73**: 651–55.
39 Fiatarone MA, O'Neill EF, Doyle-Ryan N *et al.* Exercise training and nutritional supplementation for physical frailty in very elderly people. *New Engl J Med* 1994; **330**: 1769–75.
40 Skelton DA, Young A, Greig CA *et al.* Effects of resistance training on strength, power, and functional abilities of women aged 75 and older. *J Am Geriatr Soc* 1995; **43**: 1081–87.
41 Jette AM, Harris BA, Sleeper L *et al.* A home-based exercise program for nondisabled older adults. *J Am Geriatr Soc* 1996; **44**: 644–49.
42 Maurer BT, Stern AG, Kinossian B *et al.* Osteoarthritis of the knee: isokinetic quadriceps exercise versus and educational intervention. *Arch Phys Med Rehabil* 1999; **80**: 1293–99.
43 Schilke JM, Johnson GO, Housh TJ *et al.* Effects of muscle-strength training on the functional status of patients with osteoarthritis of the knee joint. *Nurs Res* 1996; **45**: 68–72.
44 Cummings S, Phillips S, Wheat M. Recovery of function after hip fracture – the role of social support. *J Am Geriatr Soc* 1988; **40**: 861–66.
45 Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain

deficit in elderly patients. *J Am Geriatr Soc* 1975; **10**: 433–41.
46 Ware J, Kosinski M, Keller S. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; **34**: 220–33.
47 Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. *J Clin Epidemiol* 1989; **42**: 703–709.
48 Chumlea WC, Roche AF, Steinbaugh ML. Estimating stature from knee height for persons 60 to 90 years of age. *J Am Geriatr Soc* 1985; **33**: 116–20.
49 Garrow J, Webster J. Quetelet's Index (W/H^2) as a measure of fatness. *Int J Obesity* 1985; **9**: 147–53.
50 Zawada E. Malnutrition in the elderly. *Postgrad Med* 1996; **100**: 207–22.
51 Jones RH. *Longitudinal data with serial correlation: a state-space approach*. Chapman and Hall, 1993.
52 Miller M, Daniels L, Bannerman E *et al.* Adherence to nutritional supplements among patients with a fall-related lower limb fracture. *Nutr Clin Prac* 2005; **20**: 569–78.
53 Houwing R, Rozendaal M, Wouters-Wesseling W *et al.* A randomised, double-blind assessment of the effect of nutritional supplementation on the prevention of pressure ulcers in hip-fracture patients. *Clin Nutr* 2003; **22**: 401–405.
54 Paillaud E, Bories PN, Le Parco JC *et al.* Nutritional status and energy expenditure in elderly patients with recent hip fracture during a 2-month follow-up. *Br J Nutr* 2000; **83**: 97–103.
55 Albert S, Sano M, Marder K *et al.* Participation in clinical trials and long-term outcomes in Alzheimer's disease. *Neurology* 1997; **49**: 38–43.
56 Potter J, Langhorne P, Roberts M. Routine protein energy supplementation in adults: systematic review. *BMJ* 1998; **317**: 495–501.
57 Baldwin C, Parsons T, Logan S. Dietary advice for illness-related malnutrition in adults. *Cochrane Database Syst Rev* 2004; 3.
58 Milne AC, Potter J, Avenell A. Protein and energy supplementation in elderly people at risk from malnutrition. *Cochrane Database Syst Rev* 3, 2004; 3.
59 Corish CA. Pre-operative nutritional assessment. *Proc Nutr Soc* 1999; **58**: 821–29.
60 Omran M, Morley J. Assessment of protein energy malnutrition in older persons, part II: laboratory evaluation. *Nutrition* 2000; **16**: 131–40.
61 Lipski P. Australian Nutrition Screening Initiative. *Aust J Ageing* 1996; **15**: 14–17.